

REMARKS

Reconsideration is requested.

Claim 1 has been canceled, without prejudice. Claims 2-17 are pending.

Consideration of the attached Information Disclosure Statement, and the attached references, and return of an initialed copy of the attached PTO 1449 Form, pursuant to MPEP § 609, are requested. The additional references which are listed on the attached PTO 1449 Form, but not included with the Information Disclosure Statement, as noted in the same, will be filed under separate cover once received by the undersigned. The Examiner is requested to contact the undersigned in the event he next reaches the case for action and the references have not been matched with the Patent Office copy of the file, in which case the undersigned will arrange to have a further copy of the documents delivered to the Examiner.

Reconsideration and withdrawal of the restriction requirement is requested.

Consideration of the attached Rule 181 Petition in this regard is requested prior to the Examiner's next Action on the merits.

The Section 112, second paragraph, rejection of claims 5 and 16-17 is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following comments.

Claim 5 is, with all due respect, not "confusing", as asserted by the Examiner on page 3 of Paper No. 11, but rather includes the subject matter which the Examiner has withdrawn from consideration. Moreover, the recitation on "non-deleterious" in claim 16 will be recognized by one of ordinary skill in the art to refer to attachment sites to a uricase protein which do not negatively impact the circulating life or reduce

immunogenicity of the uricase protein for safe and reliable use in chronic therapy. See, for example, page 4, lines 20-22, page 6, lines 1-3 and page 14, lines 11-14, of the specification. While not believed necessary, the applicants have amended claim 16 and 17 as suggested by the Examiner on page 4 of Paper No. 11 however the scope of the claimed invention is not believed to have been affected by the amendment.

Reconsideration and withdrawal of Section 112, second paragraph rejection of claims 5 and 16-17 are requested.

The Section 101 rejection of claims 1, 2, 5 and 16-17 is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following comments.

The Examiner appears to require a statement of the utility in the compound claims to comply 35 USC 101. This is not required by the statute, rules or MPEP. The activity or utility of a compound is inherent to the compound *per se* and the law merely requires a disclosure of the utility unless the utility would be apparent from the specification or from the art.

The Examiner also asserts that SEQ ID NO:10 "does not appear to have any utility specifically stated." See, page 4 of Paper No. 11. The Examiner is urged to review however page 6, lines 16-31 of the specification wherein the uricase protein of the present invention is exemplified by the PKS amino truncated SEQ ID NO:10. See, page 6, line 28 of the specification.

The Examiner further relies on the explanation of previous unpredictability stated in page 11, lines 12 to 19 of the specification in support of the Section 101 rejection. The Examiner however has apparently failed to consider the paragraph following the

cited section of the specification (i.e., page 11, line 20 through page 12, line 3) wherein the applicants explain that it was subsequently appreciated that amino acid residue 291 of the baboon uricase is lysine but the corresponding residue in pig is arginine and that the Apal restriction site present in both cDNAs was exploited to construct a chimeric uricase in which the first 225 amino acids are derived from the pig cDNA and the carboxy terminal 79 are derived from the baboon cDNA. This passage of the specification goes on to describe the construction of the presently claimed invention and the fact that the claimed uricases are fully as active as compared to the unmutated native pig uricase in approximately more than fourfold active than unmutated native baboon uricase. The applicants submit the specification discloses a credible and specific utility for the presently claimed invention and withdrawal of the Section 101 rejection is requested.

The Section 112, first paragraph, rejection of claims 1, 2, 5 and 16-17 is obviated for similar reasons as one of ordinary skill in the art will appreciate how to make and use the presently claimed invention from the teaching of the specification as well as the art. Withdrawal of the Section 112, first paragraph, rejection is requested.

The Section 102 rejection of claims 1 and 16-17 over Miura (European Journal of Biochemistry 223, 141-146 (1994)) is, to the extent not obviated by the above, traversed. Reconsideration and withdrawal of the rejection are requested in view of the following distinguishing comments.

Claim 1 has been canceled, without prejudice such this aspect of the rejection is moot. With regard to claim 16 and 17, the cited reference fails to teach the method of claim 16 and 17 as the apparent purpose of the mutation described in the cited art is to

demonstrate that the "import activity" of urate oxidase into peroxisomes is retained when an arginine is replaced with a lysine in the SRL tripeptide at the C-terminus of urate oxidase. The cited document does not teach or suggest any aspect of the presently claimed invention relating to PEG attachment sites in a uricase protein.

Accordingly, the Section 102 rejection of claims 1 and 16-17 over Miura should be withdrawn.

The Section 103 rejection of claims 1 and 16-17 over Chau (Anal. Of Internal Medicine, New York, New York; 15 July 1988, pages 114-117) or Davis (Lancet, 8 August 1981, pages 281-283) in view of Hershfield (1991 PNAS 68, 7185-7189) is, to the extent not obviated by the above, traversed. Reconsideration and withdrawal of the rejections are requested in view of the following distinguishing comments.

The rejection insofar as it relates to claim 1 is moot as claim 1 has been canceled, without prejudice above.

With regard to claim 16 and 17, the Examiner's collection of references provides, at best, an indication that it may have obvious to try to make the presently claimed invention however as noted by the applicants on page 11, lines 12-19 of the specification, and as noted by the Examiner on pages 4 and 5 of Paper No. 11, previous attempts to introduce attachment site by site-directed mutagenesis, as described in Hershfield, when previously applied to uricase in particular, were unsuccessful. It is for this reason, for example, that the exemplified embodiments of the claimed invention, and the invention of claims 16 and 17 as a whole, are unobvious. Withdrawal of the Section 103 rejection of claims 1 and 16-17 is therefore requested.

The PTO-1449 Form returned with Paper No. 11, which contains an indication the Examiner has considered the six references cited therein on October 10, 2002, also contains an "X" through the references as the Examiner's initials in the left-hand column next to each reference. The Examiner has not initialed the left-hand margin next to the cited U.S. Patent No. 4,917,888. While the undersigned believes the Examiner has considered all the cited references, as indicated by the Examiner's signature and inclusion of October 10, 2002, as the "date considered". The Examiner is requested, for completeness, to provide a further initialed copy of the PTO-1449 Form wherein the Examiner's initials are included in the left-hand margin next to each of the cited references and the PTO-1449 Form is signed with an inclusion of the date considered, as required by MPEP §609. The applicants note these references were cited in an International Search Report dated February 2, 2000 and that the Patent Office has indicated in the Notice of Acceptance dated October 11, 2001, that the International Search Report had been received along with copies of the cited references. Nothing further should be required for consideration of these references therefore however the Examiner is requested to contact the undersigned if otherwise.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested. The Examiner is requested contact the undersigned if anything further is required in this regard.

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Respectfully submitted,
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